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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/721,839	11/25/2003	Wendy Maury	IOWA:035USD1	3197

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/721,839	MAURY ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-15 and 18-40* is/are pending in the application.

4a) Of the above claim(s) *10-15,25,26 and 29-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,9,18-24,27,28 and 34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1-20-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 1, 8-15, and 18-40 are pending in the application.

2. Applicant's election without traverse of the species of the claimed inventions wherein the antiviral peptide is SEQ ID NO: 32, the virus is HIV-1, and wherein the peptide is administered topically in the reply filed on March 11, 2005 is acknowledged. Upon further consideration, the restriction between SEQ ID NOs: 31 and 32 is withdrawn.

3. Claims 10-15, 25, 26, and 29-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 11, 2005.

4. Currently, claims 1, 8, 9, 18-24, 27, 28, 35-40 are under consideration.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on January 14, 2004 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 18-24, 27, 28, and 35-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of reducing the infectivity of enveloped viruses, does not reasonably provide enablement for methods of reducing the infectivity of any virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims read on methods of reducing viral infectivity by contacting the virus with theta defensin peptides.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, the most relevant factors are those of the presence of working examples, the state of the prior art, and the breadth of the claims.

As indicated above, the present claims are broadly drawn to methods of reducing the infectivity of any virus by contacting the virus with an anti-viral theta defensin.

In support of the claims, the application provides working examples of the claimed methods. In particular, the application demonstrates that the theta defensins identified as RTD-3

and HTD-1 both had anti-viral effects in vitro against an enveloped virus (HIV). Page 44. In addition to these teachings by the application, the art teaches that defensins, including theta defensins, kill microorganisms through permeabilizing pathogen cell membranes. See e.g., Lehrer et al., U.S. 6,713,078, columns 1-2; and Risso et al., J Leuk Biol 68: 785-92, abstract (both references of record in the January 2004 IDS). While recognizing the antimicrobial activity of these peptides generally, with regards to viruses, the art limits its acceptance of the antiviral activity towards enveloped viruses. Risso, page 785, left column, last paragraph. Thus, neither the art, nor the specification teaches that theta defensins may be used to reduce the infectivity of viruses other than enveloped viruses.

In view of the lack of any demonstration of that the identified anti-viral peptides are effective against non-enveloped viruses, and the teachings in the art suggesting that the peptides would only be effective against enveloped viruses, the application has not provided sufficient information to enable the practice of the claimed method with respect to non-enveloped viruses. The claims are therefore rejected for exceeding the scope of enablement.

8. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This claim is directed to embodiments of the claimed method for reducing viral infectivity wherein the subject is latently infected with the target virus. The application has not enabled the practice of this embodiment.

In this instance, the relevant factors from those set forth above are the nature of the claimed invention, the state of the prior art, and the presence of working examples. In the present application, there does not appear to be any demonstration that the theta defensins used in the claimed methods are effective for reducing the infectivity of viruses in latent infections.

However, the art does provide relevant teachings. In particular, the art indicates that the theta defensins kill microorganisms through permeabilizing pathogen cell membranes. See e.g., the teachings of Lehrer and of Risso, each of which was cited above. Thus, the art indicates that the efficacy of the claimed methods depends on the defensin peptides ability to interfere with the envelope of the viral particles. However, it is known in the art that latent infections are due to the presence of viral DNA or RNA inside infected cells. See e.g., Ho, Science 280: 1866-67; and Chun et al., PNAS 96: 10958-61 (each teaching the mechanism of HIV-latency- i.e. the presence of inactive by replication competent viral nucleic acids in latently infected cells). There is no viral envelope in such latent infections for the defensins to interfere with. It is noted that an additional anti-HIV function has been discovered for certain defensins. See e.g., Munk et al., AIDS Res Human Retrovir 19: 875-81 (teaching that certain theta defensins can inhibit HIV binding to target receptors). However, this mechanism for anti-viral activity is also effective against only active infection, and not against a latent infection. Thus, there has been no disclosure of any mechanism by which the peptides could interfere with the infectivity of such latent infections. In view of the teachings of anti-viral mechanism of the defensins, and the lack of any evidence or demonstration that such peptides would be effective in reducing the infectivity of latent infections, the application has not enabled those in the art to practice the method of claim 39.

9. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim has been described above. It reads on a genus of inventions comprising reducing the infectivity of latent viral infections through the administration of a theta defensin peptide.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. However, even the presence of multiple species with in a claimed genus does not necessarily demonstrate possession of the genus. See, In re Smyth, 178 U.S.P.Q. 279 at 284-85 (CCPA 1973) (stating "where there is unpredictability in performance of certain species or subcombinations other than those

specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus or combination claimed at a later date in the prosecution of a patent application."); and University of California v. Eli Lilly and Co., 43 USPQ2d 1398, at 1405 (Fed Cir 1997)(citing Smyth for support). Thus, where there is uncertainty in the operability of species other than those disclosed, even the presence of working examples within a claimed genus would not necessessarily demonstrate possession of the claimed genus.

As indicated above, the rejected claim is drawn to a genus of methods for the reduction of the infectivity of a latent viral infection with a theta defensin. While the application has provided examples demonstrating the inhibition of infectivity in active infections, there has been no demonstration by the application that the peptides would be effective against latent infection. Further, as described above, the art provides teachings that render uncertain the ability of theta defensins to be active against latent viral infections, as the peptides are active against viral envleopes (not present in latent infections) and occasionally against viral binding to cell receptors (against, only present in active infection). In view of the failure of the application to demonstrate possession of a method for the treatment of a latent infection by theta defensins, and the uncertainty caused by the teachings in the art as to the ability of the peptides to act against such latent infections, the Applicant has not provided sufficient written description support to demonstrate possession of the method of claim 39.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1, 8, 9, 18-24, 27, 28, 35-38, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Lehrer et al., WO 02/085401. These claims are directed to methods of reducing the infectivity of a virus, particularly HIV, through administration of the peptide of SEQ ID NO: 32, with or without additional anti-viral agents.

Lehrer teaches the making and use of theta defensins comprising an amino acid sequence formed from any combination of two nonapeptides selected from those disclosed as SEQ ID NOs: 19-64 in the reference. See e.g., claim 6. Among the nonapeptides disclosed by the reference are those of SEQ ID NOs: 27, 31, and 34. The theta defensin formed by the combination of SEQ ID NOs: 31 and 34 would be identical to the defensin of SEQ ID NO: 32 in the present application. The defensin comprising SEQ ID NOs: 27 and 34 would result in the defensin of SEQ ID NO: 31. The reference additionally teaches that these defensins may be administered to a subject with a viral infection, facing exposure to viral infection, including infection by HIV. Pages 13-14. The reference teaches that the defensins may be applied topically (page 13, lines 31-32), and may be applied in combination with other antiviral agents (pages 17-18). While the reference does not teach the specific dosages for the defensins, the reference indicates that such dosages would vary based on several factors (page 16, lines 24-30), and thereby indicating that the claimed dosages would be obvious based on routine optimization of the disclosed compositions.

While the reference does not specifically teach the peptide according to SEQ ID NO: 32, as indicated above, the reference teaches that any of the defensins formed by the combination of any two of the disclosed nonapeptides, including SEQ ID NOs: 31 and 34, would be effective in the indicated uses. Thus, because the reference renders obvious all of the indicated peptides, the reference would render obvious the use of any one of them. It is further noted that the present application provides no further suggestion as to why this particular peptide was chosen, or any indication that the instant methods of using the peptide have any non-obvious features (e.g., that the peptide of SEQ ID NO: 32 is particularly efficacious in the claimed methods). The same applies to the teachings regarding SEQ ID NOs: 27 and 34 in the reference in rendering the use of SEQ ID NO: 31 in the present claims obvious. The teachings of the reference therefore render the claimed methods obvious.

With respect to claims 35-38 and 40, the teachings of Lehrer indicate that the theta defensins act directly against the virus, and would therefore be suitable for use in immunocompromised patients. Further, as was indicated above, the reference teaches that the defensins may be administered to a subject with a viral infection or facing exposure to viral infection. Thus, the reference indicates that the peptides may be administered both to inhibit infection, and to reduce the infectivity of viruses in patients with active viral infections. The references therefore render the limitations of claims 35-38 and 40 obvious.

It is noted that this reference has a filing and a publication date after the present application's earliest claimed priority date. However, the reference claims priority to an earlier U.S. provisional application filed on April 18, 2001. In addition, although the present application claims priority to application 60/265,270, filed on January 30, 2001, this earlier application does

not provide support for the presently claimed methods. I.e., there is no support in the application for the peptide of SEQ ID NO: 32.

Conclusion

12. No claims are allowed.

13. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Tang et al., Science 286: 498-502 (of record in the January 2004 IDS). This reference teaches a primate theta defensin comprising the sequences corresponding to SEQ ID NOs: 27 and 3 in the Lehrer et al. reference (WO 02/085401) above. These sequences represent the monkey portions of the chimeric defensins of SEQ ID NOs: 31 and 32 in the present application. However, Tang does not teach the combination of these subsequences within the monkey theta defensin with the human versions of the subsequences so as to render the claimed inventions obvious.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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